Screening for neurocognitive deficits in adult populations reliant on toxic cassava as the main source of food

Dépistage des déficits neurocognitifs dans les populations adultes dépendant du manioc toxique comme principale source de denrées alimentaires

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Résumé

Contexte & objectif. La dépendance alimentaire chronique au manioc cyanogène mal détoxifié est largement répandue en Afrique subsaharienne. L'objectif de la présente étude était de dépister les troubles neurocognitifs et le fonctionnement de la vie quotidienne chez les adultes avec dépendance alimentaire au manioc cyanogène comme principale source de nourriture. Méthodes. C'était une étude transversale analytique incluant les chefs de ménage vivant dans le district rural de Kahemba, en République démocratique du Congo. Les participants ont été dépistés pour les troubles neurocognitifs à l'aide de Community Screening Interview for Dementia (CSID). L'exposition au manioc cyanogène a été déterminée par les concentrations urinaires de thiocyanate (SCN). Des modèles de régression ont été utilisés pour identifier les prédicteurs de mauvaises performances au CSID. Résultats. Quatre cent et six chefs de ménage (203 couples, âge moyen 38,4 ± 11, 4 ans) ont été enrôlés. Cent trente-six (33,5 %) [69 femmes et 67 hommes, âge moyen 39 ± 14,4, ans et 13 (3,2 %) [7 femmes et 6 hommes, âge moyen 32 ± 2,6 ans,) remplissaient respectivement les critères de trouble neurocognitif léger (TNL) et de trouble neurocognitif majeur (TNCM). La concentration urinaire Moyenne globale de SCN était de 949,5 ± 518,3 µmol/L. Après ajustement pour l'âge, le sexe, l'état nutritionnel et les antécédents de konzo, les déficits spécifiques aux différents domaines de la neuro-cognition étaient significativement associés de manière

Summary

Context and objective. Chronic dietary reliance on improperly processed cyanogenic toxic cassava is widespread in sub-Saharan Africa. The objective of the present study was to screen for neurocognition impairments and daily-life functioning in adults with dietary dependency on cyanogenic cassava as the main source of food. Methods. A cross-sectional design enrolled heads of households (in couples) in the rural district of Kahemba, Democratic Republic of Congo. Participants were screened for neurocognitive impairments using the Community Screening Interview for Dementia (CSID). Detailed neuropsychiatric evaluations were performed and disease entities classified according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria when applicable. Cassava cyanogenic exposure was ascertained by urinary concentrations of thiocyanate (SCN). Regression models were used to identify predictors of CSID performance at the 0.05 significance level. Results. For hundred and six households (203 couples, mean age 38.4 ± 11. 4 years) were involved. One hundred thirty-six subjects (33.5 %) [69 women and 67 men, mean age 39 ± 14.4 years)] and 13 (3.2 %) [7 women and 6 men, mean age: 32 ± 2.6 years] fulfilled the criteria for mild cognitive impairment (MCI) and Major Neurocognitive disorder (MNCD), respectively. The overall mean urinary concentration of SCN was 949.5 ± 518.3 ☐mol/L. After adjusting for age, gender, nutritional status, and history of konzo, neurocognition domain-specific deficits were independently associated with either hypertension or USCN (350 ☐mol/l incremental increase in excretion). Functional impairments in daily-life activities increased as subjects poorly performed at the CSID screening (Spearman r = - .2, p < 0.01).
Conclusion. Neurocognitive deficits in adults are

indépendante à l'hypertension ou à l'USCN (350 µmols/L, augmentation incrémentale de l'excrétion). Les déficiences fonctionnelles dans les activités de la vie quotidienne ont été directement proportionnelles à la mauvaise performance au CSID (Spearman r = - 0, 2, p < 0,01). Conclusion. Les déficits neurocognitifs sont courants chez les adultes congolais qui dépendent du manioc cyanogène comme principale source de nourriture. Ce qui justifie la réalisation d'études ultérieures pour élucider l'impact cérébral / comportemental global ainsi que les mécanismes de la toxicité du manioc chez les adultes ayant une dépendance alimentaire au manioc cyanogène.

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common in Congolese adults relying on cyanogenic cassava as the main source of food. Our study findings warrant further studies to elucidate the overall lifespan brain/behavioral burden and mechanisms of cassava toxicity among adults with dietary dependency on cyanogenic cassava as the main source of food.

Introduction

Chronic reliance on cyanogenic cassava in the settings of hunger, inadequate detoxification of its tubers, or yet to be fully documented individual susceptibility, can lead to neurological impairments and disability. These include acute encephalopathy, sub-acute spastic para paresis (a.k.a. konzo), tropical ataxic neuropathy (TAN), and/or, reportedly, a cerebellar-parkinsonism-dementia syndrome (CPDS) (1-3). Outbreaks of konzo have since occurred in several countries of sub-Saharan Africa including Angola, Cameroon, Central African Republic, Democratic Republic of the Congo (DRC), Tanzania, Uganda, Mozambique, and recently in Zambia (4-6). Konzo was named after a local designation in *kiyaka*, a local language spoken in DRC and means "tied legs" in reference to the scissoring spastic gait of affected subjects (6). Children and women of childbearing age are at higher risk for reasons that have yet to be known (8-10).

Impoverished populations in rural Africa are at risk for the aforementioned neurological diseases because of their dietary dependency on food from drought-tolerant varieties of cassava a.k.a tapioca or yucca, which contain high concentrations of two cyanogenic glucosides notably linamarin and lotaustralin, in a ~97:3 concentration ratio (11-12). Overt diseases e.g. konzo or TAN surface when toxic thresholds are exceeded and subjects have limited detoxification capabilities because of low dietary protein intake (13). Cassava toxicity is commonly seen in times of famine often caused by flood, drought, pestilence, or war. In these times, poor populations are forced to adopt shortcuts in processing methods including a reduction in cassava processing time. Under these conditions, higher residual amounts of cyanogenic compounds are ingested and first converted into cyanide, a highly toxic compound. Naturally, defense mechanisms would then convert cyanide into the purportedly less toxic thiocyanate (SCN) which in turn is excreted in urine making it a suitable marker of food (cassava) cyanogenic exposure (12).

Neurological effects of food dependency on cassava represent a significant contribution to the global burden of disease. Unofficial estimates indicate that up to 100,000 cases of konzo may

have already occurred across the African continent (14). We also showed that cognition may be impaired in addition to the paralysis in children with konzo and those with no overt paralysis still perform worse at neuropsychological testing compared to children from non-konzo areas suggesting that pervasive cognition deficits have commonplace in konzo-affected areas (10, 15-16). Whether poor cognition may extend into adolescent and adult life impacting functioning and economic productivity still needs to be determined. In this study, we screened for dementia in the adult population of Kahemba, a konzo heavily affected district of the Democratic Republic of Congo (DRC), which relies on cassava farming for its subsistence (7, 9) and draw attention to a high prevalence of mild cognitive impairments (MCI) in this population.

Methods

Study Population. The present study was carried out in the district of Kahemba, southern Bandundu, nowadays the Kwango Province of the DRC. Residents of Kahemba heavily rely on cassava farming and possess very limited livestock for subsistence. During the last decade, Kahemba has faced a severe humanitarian crisis due to population displacement following the end of the Angola war. Because of food shortages, residents were forced to adopt shortcuts in cassava processing methods, a phenomenon that led to food cyanogenic exposure and poisonings. A sudden rise in the number of cases with konzo was since documented with a point-prevalence of the disease as high as 20% in certain villages (17).

Study Design. We carried out a cross-sectional study that consecutively enrolled household consenting members. Source population: these subjects are parents of children enrolled in previously studies that assessed cassava toxicity and neurodevelopmental outcomes in Kahemba (10). Inclusion criteria: only consented heads of households and couples who were permanent residents of Kahemba participated were included. The vast majority of the subjects (96 %) lived in Kahemba prior to the 2009 major outbreak of konzo (7). Exclusion criteria: subjects with a

history of neurological disability and/or mental illnesses were excluded from the study.

Data collection tools and parameters of interest
A questionnaire was used to collect data on sociodemographic characteristics, medical history, and current health status. Cognitive impairment, anxiety and/or depression, neurological evaluation, and cassava cyanogenic exposure, were assessed using tools that are outlined below. Cognition status was the main outcome variable, of which changes were assessed in relation to sociodemographic, clinical status, nutrition and cyanogenic exposure levels.

Cognitive Status, Functioning, and Depression Screening
The community screening interview for dementia (CSID) developed to screen for dementia across cultures and resource settings was used for study purposes (18). The CSID consists of a set of direct cognitive screening tasks for non-literate and literate populations, in addition to an assessment of the everyday functional status through an interview with a close informant. An overall cognitive score is calculated which ranges from 0 to 34 with lower scores indicating cognitive impairment. A cutoff point of CSID score < 25 was considered as the threshold for cognitive impairment in this study (19-20). The informant score ranges from 0 to 40 with scores > 16 indicating functional impairments in everyday life activities. Study participants were further examined by a certified Congolese neuropsychiatrist and classified as having either normal cognition, or mild cognitive impairment (MCI), or dementia based on the criteria listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV). Signs indicative of depression and/or anxiety were assessed through a structured interview using the Goldberg Depressive Anxiety Scale (GDAS), an instrument previously used in the DRC (21); a GDAS score ≥ 22 was indicative of the depressed mood. The severity of the tendency to depression was graded as mild (scores 22 - 35), moderate (scores 36 - 53), or severe (scores ≥ 54).
Neurological Evaluation. A Congolese board-certified neuropsychiatrist performed

neurological examinations on all subjects to assess cranial nerves, motor and sensory functions as well as reflexes and sphincter control. The diagnosis of konzo (cassava-associated spastic paraparesis) was based on the following WHO criteria for the disease: (1) a visible symmetric spastic abnormality of gait while walking or running; (2) a history of onset of less than 1 week followed by a non-progressive course in a formerly healthy person; and (3) bilaterally exaggerated knee or ankle jerks without signs of disease of the spine (22). Anthropometric measurements (height, weight, mid-upper arm circumference) were also made at the time of the neurological evaluation to determine nutrition status as a function on body mass index (BMI).

Ascertainment of Cassava Cyanogenic Exposure
During the initial visit to Kahemba, samples of cassava flour from 18 consenting households were collected and found to have cyanide concentrations of 30 to 200 ppm, well-above the 10-ppm safe limit proposed by the WHO (23). We have previously reported higher levels of urinary SCN in children with konzo relative to their respective controls from our study area (15, 24). In the present study, urine samples from study participants were analyzed using the same previously used urinary SCN picrate measurement D1kit. In this analysis, a color chart is used with 10 shades of color from yellow to brown, corresponding to 0–100 mg SCN/l urine (ppm). The results in ppm are then multiplied by 17.2 to convert to μmol SCN / l according the manufacturer protocol (25).

Ethics statement
Informed consent was obtained verbally by investigators fluent in Lingala and/or Kikongo, the local spoken languages. The research protocol was approved by the Institutional Review Board of the DRC Ministry of Health.

Statistical Analyses
Initial analyses consisted of Student t-tests, as well as Chi-square tests to compare key clinical and biological characteristics across study groups as deemed appropriate. Logistic regression was first used to assess relationships between neurocognitive status (CSID normal score ≥ 25vs. CSID poor score<25) and age, gender, body mass index (≤ 18.4kg/m^2 for malnutrition), systolic and diastolic blood pressure, glycemia, smoking, alcohol consumption, depression, functioning, neurological and konzo status, and urinary concentrations in SCN as independent variables. Predictors significantly associated to the main outcome at the .10 significance threshold were then retained in models for multivariable analyses that assessed the aforementioned associations after adjusting for age, gender, nutrition status, exposure levels, konzo status and/or hypertension at the .05 significance level. All analyses were carried out using the STATA software (STATA, STATA inc. version 16.1).

Results
*Sociodemographic Characteristics of Study Subjects*
Of the 406 study participants (203 household couples; men/women ratio: 1/1), the majority (42%) were aged between 31 and 45 years regardless of gender and the 61 – 75 age group (12 subjects) was the least represented group making 3% of the study subjects. Most subjects (84.7 %, overall) had post-elementary education regardless of gender. The average (SD) duration of stay in Kahemba was 33.3 (13.9) years and most subjects (**96.6** %) have been living in Kahemba prior to the major 2019 konzo outbreak.

Clinical and Biological Characteristics of Study Subjects
More than half of the subjects (54%, overall) suffered chronic undernutrition. Alcohol consumption was reported in 267 (65.8 %) subjects. Overall, fewer subjects (6.7 %) had hypertension, hyperglycemia (13.5 %), and smoking habits (5.9%). Subjects were heavily exposed to cassava cyanogens as indicated by concentrations of urinary SCN above 350 μmol/l in the majority (78%) of subjects regardless of gender. Of the total 406 study participants, 240 (59.1 %) subjects had at least one subject with konzo in their households while 38 (9.4 %) (26 men and 12 women) had konzo themselves.

CSID performance scores followed a normal distribution (**Figure 1**.). Depressed mood was reported in 258 (63.5 %) of the study participants, almost exclusively in the group that performed well at the CSID screening. Of these, 135 were prone to mild depression, 97 to moderate, 26 to severe depression as per the Golberg scale.
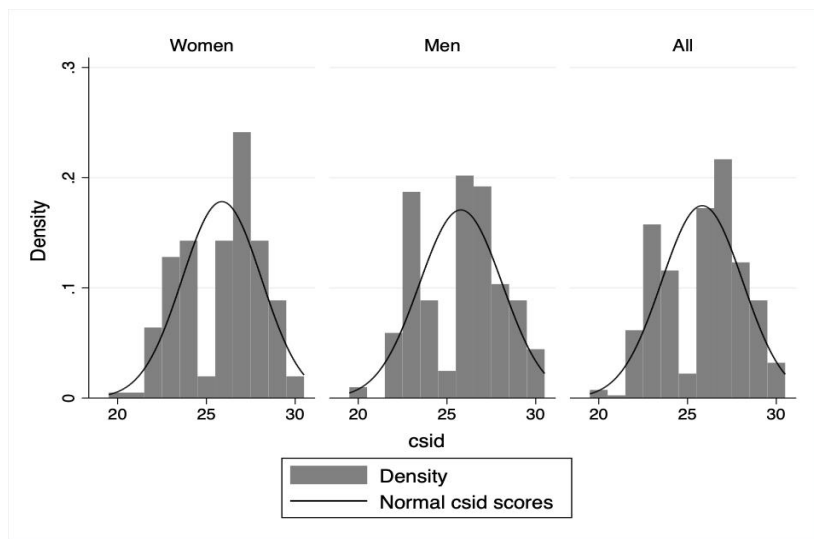
One Hundred forty-nine (36.7 %) subjects poorly performed at the CSID screening. One hundred thirty-six (33.5 %) [69 women and 67 men, mean (SD) age39 (14.4), range 18 – 73 years) and 13 (3.2 %) [7 women and 6 men, mean (SD) age: 32 (2.6) years, range 27 - 36) fulfilled the criteria for MCI and dementia, respectively. Key clinical and biological characteristics across study groups are summarized in **Figure 2** and **Table 1**.

Figure 1. Performance scores at the CSID screening followed a normal distribution regardless of gender.
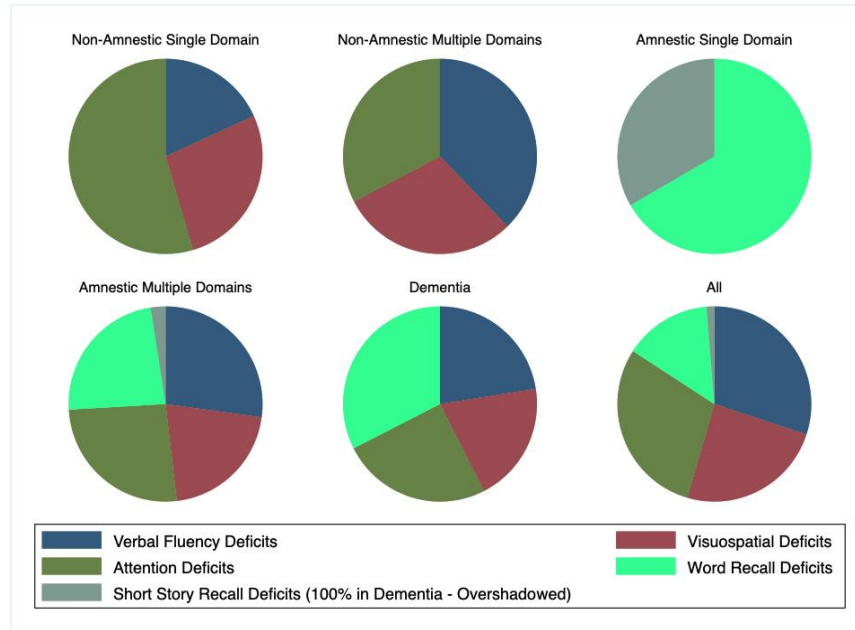
Figure 2. Patterns of neurocognition status showed several domains affected at neurological screening.

Clinical and Biological Predictors of CSID status
Increases in urinary thiocyanate excretion (by 350 micromol/l and HT were associated with domain-specific neurocognitive impairments. By removing the HT (predictor of non-amnestic multidomain deficits) from the model, increase in urinary thiocyanate excretion remained a significant predictor of most deficits except for the non-amnesic unidomain impairment (Table 2).

Table 2. **Clinical and Biological Predictors of Neurocognition Status** (Univariable multimodal logistical regression of risk factors of neurocognitive impairment by type of disorder)

Predictors	MCI (n=136)				MNCD (n=13)
	Non amnesic		**Amnésic**		
	Single unidomain OR (95% CI)	**Multidomain** OR (95% CI)	**Single unidomain** OR (95% CI)	**Multidomain** OR (95% CI)	
Age/year	0.96 (0.89-.1.04)	0.9 (0.9 -1.03)	0.93 (0.77-1.12)	1.00 (0.97-1.04)	**0.93 (0.82 -1.04)**
Men	0.69 (0.15-3.15)	1.5 (0.6 -3.5)	1.37 (0.9-0.0)	0.79 (0.37-1.69)	0.46 (0.07-3.29)
Undernutrition (BMI ≤ 18.4 kg/m^2)	0.24 (0.04 -1.33)	1.9 (0.7 -4.6)	0.41 (0.02-7.79)	1.01 (0.47-2.20)	0.39 (0.06-2.62)
Thiocyanate /350 µmol/l	0.49 (0.2 -1.07)	**2.3 (1.6 -3.2)**	**0.02 (0.00-0.96)**	**0.70 (0.5-0.97)**	**2.18 (1.07-4.45)**
Konzo in households	2.04 (0.37 -11.14)	0.72 (0.3-1.6)	18.56 (0.7- 437.0)	2.12 (0.93-4.87)	0.43 (0.06 -2.99)
Hypertension	--	**7.7 (1.5-39.0)**	71.7 (0.1-4742.6)	4.43 (0.85-22.99)	--
		By moving out HT in the model			
Age/year	0.96 (0.89-.1.04)	1.00 (0.9-1.04)	0.98 (0.87-1.12)	1.01 (0.98-1.04)	0.93 (0.82 -1.04)

Men	0.67 (0.15-3.06)	1.4 (0.6 -3.34)	-	0.81 (0.38-1.73)	0.47 (0.07-3.32)
Undernutrition (BMI ≤ 18.4 kg/m^2)	0.24 (0.04 -1.33)	1.79 (0.7 -4.3)	0.34 (0.02-5.13)	0.94 (0.44-2.02)	0.40 (0.06-2.65)
Thiocyanate /350 µmol/l	0.48 (0.22 -1.05)	**2.3 (1.6 -3.21)**	0.0 (0.0-0.9)	**0.72 (0.52 -0.99)**	**2.17 (1.07-4.43)**
Konzo in households	2.06 (0.38 -11.1)	0.71 (0.3-1.6)	20.4 (1 - 416.15)	1.97 (0.87-4.47)	0.41 (0.06 – 2.8)

Legend: OR = Odd Ratio at multinomial logistic regression; n = number, BMI = Body Mass Index; MCI = Mild Cognitive Impairment. MNCD = Major Neurocognitive Disorder; HT = Hypertension.

Impairments in daily living activities increased as performance at the CSID decreased (Spearman r = - .2, p < 0.01), figure 3.
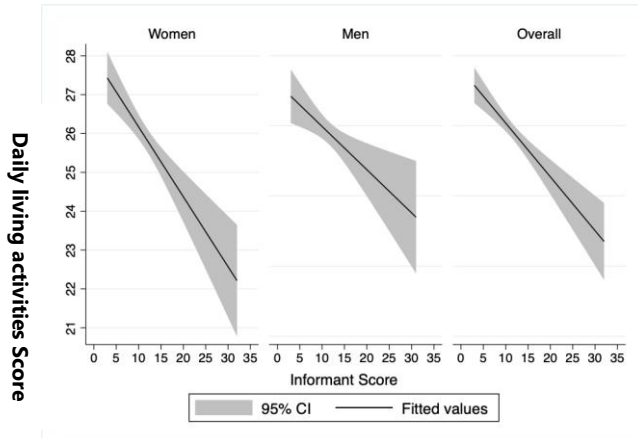

Figure 3. Impairments in daily living activities increased as performance at the CSID decreased both in women and in men, and overall.

Discussion

The main purpose of this study was to assess cognitive status and daily life functioning of adults relying on cyanogenic cassava as the main source of food. One hundred thirty-six (33.5 %) and 13 subjects (3.2 %) had MCI and dementia, respectively. Patterns of neurocognition functioning showed several domains (verbal fluency, attention, memory, and/or visuo-spatial processing) affected at neurological screening. The very high proportion of MCI (33.5 %), with overt impact on functioning, raises serious concerns on economic productivity in konzo-affected areas (26).

We have previously conducted electrophysiological and neurodevelopmental studies that suggested neurocognitive deficits in konzo (10, 27). Preschool-children, school age children, and adolescent have neurodevelopmental disabilities associated with cassava cyanogenic exposure (10, 15-16). This study provides the first systematic attempt to determine whether cognition may be affected in

adults relying on cyanogenic cassava as the main source of food. The prevalence of dementia (3.2 %) is similar to those from studies across rural sub-Saharan Africa (28) suggesting no or little impact of the cyanogenic diet on the occurrence of dementia. The association between domain-specific cognition deficits and levels of urinary SCN is a significant finding, as it appears to be consistent of findings from other studies conducted in sub-Saharan Africa suggesting possible neurotoxicity links (2, 10, 15-16, 29-30). However, a robust study design with markers of direct cyanide load (e.g., blood cyanide) and metabolism of sulfur amino acids would provide clear insights on whether excretion of urinary SCN is either a sign of marked toxicity or a sign of protective mechanisms against cyanide toxicity. The high proportion of depressed mood and/or the impact of hypertension on cognition as revealed in our study population, despite a small number of subjects with the condition, warrant further investigations. This present study remains, however, an important step in revealing the extent to which cognition and daily life

functioning may be affected among heavy cassava reliant populations; providing insights into the existence of preventable causes of cognition deficits among these populations.

Global Health Importance and Perspectives
Neurocognitive deficits in adults are common among Congolese adults who depend on cyanogenic cassava as their primary food source. Much of sub-Sahara Africa is becoming increasingly dependent on high-yield varieties of cassava that thrive in ecological degraded zones. Cassava is increasingly used as food-thickening ingredient. It is also exported to feed animals and produce snack for human consumption. Therefore, it is critical to continue brain/behavior research that will help us better understand its neurotoxic properties. Longitudinal studies, combined with studies of more sensitive biomarkers of neuropathogenesis, will help determine whether neurocognitive deficit is on a cassava-associated continuum of neurodegeneration and whether neurodevelopmental deficits in younger populations extend into adulthood.

Strengths and weaknesses of the study
This study is the first demonstration, in adults from an environment affected by konzo, of an obvious link between putative neurocognitive deficits and cassava cyanogenic exposure. Causal relationships may not be established due to lack of reliable markers of blood cyanide load and limits inherent to cross-sectional designs. Longitudinal studies will help determine whether MCI is on a continuum of a cassava-associated neurodegeneration and/or whether neurodevelopmental deficits in younger populations extend into adulthood.

Conflict of interest statement
Authors have no conflicts of interest to report.

Author contributions
Victor Hutu, MD, University of Kinshasa, participated in the field testing and drafting of the manuscript.

Daniel Okitundu, MD PhD, University of Kinshasa, participated in the field testing, analysis of data, and drafting of the manuscript.
Michael JBoivin, PhD MPH, Michigan State University, participated in the design of the study, analysis of the data, and drafting of manuscript.
Bruno Giordani, PhD, University of Michigan, participated in data analysis and drafting of manuscript.
Dieudonné Mumba MD PhD, Institut National de Recherches Biomédicales, participated in the study design, biochemical analyses, and drafting of manuscript.
Desire Tshala-Katumbay, MD PhD, Oregon Health and Sciences University, was the study principal investigator, participated in the design of study, oversight of neurological exam and data analysis, and drafting of the manuscript.

Table 1. Clinical and biological characteristics of study by gender and cognition status

Legend: % = percentage; N/n = Number; SD= Standard Deviation. N = Number, SBP = Systolic blood Pressure. DBP=Diastolic blood Pressure.

Variables	All (N=406)	Men (N=203)	Women (N=203)	CSID ≤ 25 (Impaired N=149)	CSID > 25 (Normal N=257)	MCI (N=136)	Dementia (N=13)
Mean (SD) age	38.37 (11.12)	39.33 (10.96)	37.41 (11.21)	38.35 (9.2)	38.4 (13.9)	39 (14.4)	32.1 (2.6)
Men (n, %)	203 (50)	203 (50)	-	75(18,5)	128(31,5)	69(17)	6(1,5)
Women (n, %)	203 (50)	-	203(50)	74(18,2)	129(31,8)	67(16, 6)	7(1,7)
post-primary education level	344 (85)	180 (44.3)	164 (40.4)	126 (31.0)	218 (53.7)	115 (28.3)	11 (2.7)
Mean (SD)BMI (kg/m^2)	18.83 (3.1)	18.7 (2.9)	19 (3.3)	18.7 (3.0)	18.9 (3.0)	18.7 (3.0)	18.6 (2.0)
Undernutrition (BMI ≤ 18.4 kg/m^2)	220 (54, 2)	115(28,3)	105(25,9)	82(20,2)	138(34)	75(18,5)	7(1,7)
Mean (SD) SBP (mmHg)	118 (20.5)	117.8 (20.3)	118.25 (20.5)	115 (16.3)	119.8 (21.5)	114.6 (15.9)	118.9 (21.0)
Mean (SD) DBP (mmHg)	71.5 (13.1)	71.4 (13.2)	72 (13)	68.4 (11)	73.3 (13.8)	68 .1 (11)	71.5 (13.4)
Hypertension (n, %)	19(4, 7)	10 (2,5)	9(2, 2)	*14(3, 4)	*5(1,23)	*14(3, 4)	*0(0)
Mean (SD) Glycemia (mg %)	89.78 (35)	88.3 (33.2)	91.3 (36.8)	89.19 (34)	90.2 (34.6)	90.2 (37)	76 .7 (15)
Hyperglycemia (n, %)	55(13, 5)	26(6,4)	29(7, 1)	20(4, 9)	35(8, 6)	19 (4.7)	1(0,2)
Smoking (n, %)	24(5, 9)	13(3, 2)	11(2,7)	13(3,2)	11(2,7)	10 (0.5)*	3 (0.7)*
Alcohol consumption (n, %)	267(65,8)	135(33,3)	132(32,5)	98(24,1)	169(41,6)	89 (21.9)	9 (2.2)
Konzo subject (n, %)	38(9,4)	26(6,4)	12(2,9)	16(3,9)	22(5,4)	15 (3.7)	1(0,2)
Palmomental reflex (n, %)	349(86)	172 (42,4)	177(43,6)	*135(33,3)	*214(52,7)	124 (30.5)	11(2,7)
Snout reflex (n, %)	205 (50,5)	110 (27,1)	95(23,4)	77(19)	128(31,5)	69 (17)	8 (2)
Mean (SD) USCN (µmol/l) (N= 242)	949.6 (518.3)	961.9 (534)	935.25 (501.5)	€1049(479.7)	€889.62 (532.8)	€1050.4 (479.1)	€1032(525.5)
USCN 100 – 350 (n, %)	54(22,3)	32(13,2)	22(9,1)	17(7)	37(15,3)	17(7)	0
USCN > 350 (n, %)	188(77,7)	98(40,5)	90(37,2)	71(17, 5)	117(48,3)	66(27.3)	5(2,1)
Mean (SD) CSID Score	25.8 (2.3)	25.8 (2.4)	25.8 (2.2)	23.2 (0.9)	27.4 (1.2)	23.2 (1.0)	23 (0.6)
Mean (SD) Golberg Score	29.6 (14.0)	29.37 (13.3)	29.8 (13.9)	15.6 (3.8)	37.6 (10.6)	16(3.4)	15(3.2)
Depressed Mood (n, %)	258(63,5)	129(31,8)	129(31,8)	1(0,2)	257(63,3)	1(0,2)	0(0)
Mean (SD) informant score	16.8 (8.7)	19.37 (8.8)	14.18 (7.8)	21.5 (8.4)	14.1 (7.7)	21.1 (8.6)	23(0.6)
MCI (n, %)	136(33.5)	69(17)	67(16, 6)	136(33.5)	-	136(33.5)	-
Dementia (n, %)	13(3,2)	6(1,5)	7(1,7)	13(3,2)	-	0	13(3,2)

USCN=Urinary concentration of Thiocyanate.MCI = Mild Cognitive Impairment. MNCD = Major Neurocognitive Disorder. * = significant difference in khi-square test. ¢ = significant difference in Student's test-t. BMI=Body Mass Index, Goldberg Score ≥ 22 = Depressed Mood, CSID Score < 25 = Cognition Deficit.

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